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Electrophilic Heterocyclization of 6-Alken(yn)ylsulfanyl-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones

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Abstract—6-Allylsulfanyl-1-arylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones react with iodine and sulfuric acid to give angular pyrazolothiazolopyrimidine derivatives. The reaction of 6-(prop-2-yn-1-ylsulfanyl)-1-(4-tolyl)-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one with sulfuric acid gives angularly fused pyrazolo[4,3-*e*][1,3]thiazolo-[3,2-*a*]pyrimidin-4-one, whereas in the reaction with sodium methoxide linearly fused pyrazolo[3,4-*d*][1,3]-thiazolo[3,2-*a*]pyrimidin-4-one was formed. Linearly fused pyrazolo[3′,4′:4,5]pyrimido[2,1-*b*][1,3]thiazole derivatives were also obtained by reaction of 1-aryl-6-(3-phenylprop-2-en-1-ylsulfanyl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones with sulfuric acid.

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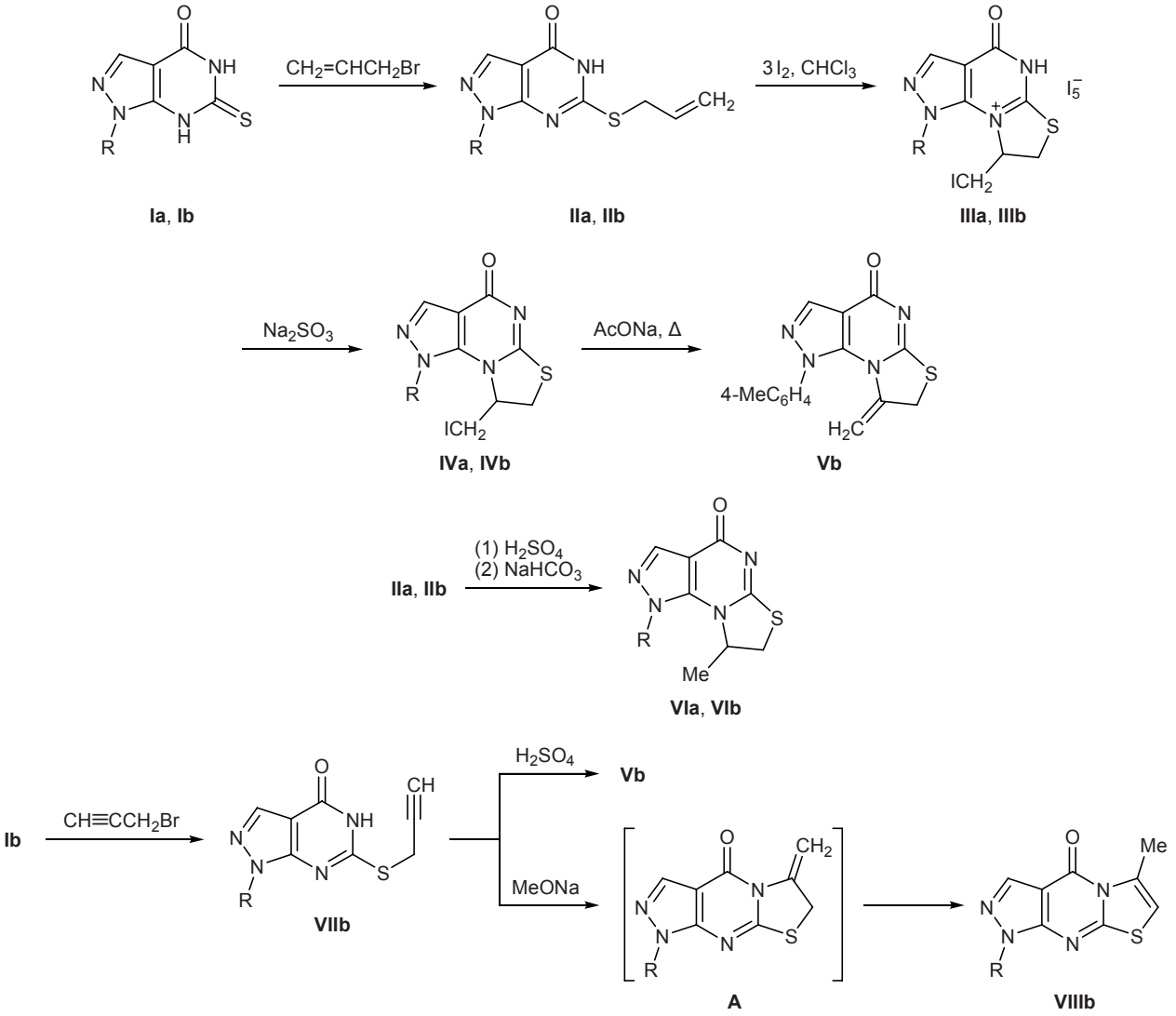
Pyrazolo[3,4-*d*]pyrimidines are structural isomers of purine; they have attracted increased researchers' attention due to the fact that some pyrazolo[3,4-*d*]-pyrimidine derivatives were found to act as adenosine receptor antagonists [1, 2]. Biological activity of pyrazolo[3,4-*d*]pyrimidines is determined primarily by the nature of substituents on N^1, C^4, and C^6 [3–5]. Therefore, we believed to be important to obtain previously unknown 6-alkenylsulfanyl- and 6-alkynylsulfanyl-substituted pyrazolo[3,4-*d*]pyrimidines and, with account taken of relations revealed in [6–8], use them in the synthesis of new derivatives of the tricyclic pyrazolothiazolopyrimidine system. Despite limited number of known representatives of this series, effective calcium channel blockers [9] and compounds possessing a strong antiphlogistic activity [10] were found among these compounds.

As starting compounds we selected 6-thioxopyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **Ia** and **Ib** which were prepared according to the procedure described in [11]. By reaction of **Ia** and **Ib** with allyl bromide we obtained 6-allylsulfanylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **IIa** and **IIb** (Scheme 1). Molecules **IIa** and **IIb** possess two nucleophilic centers (N^5 and N^7 atoms in the pyrimidine ring) which can be involved in intramolecular electrophilic cyclization. Insofar as these centers are nonequivalent (the N^7 atom seems to be preferred for ring closure [6–8]), we tried to equalize their reactivities via introduction of a bulky aryl substituent into position *1* of the pyrazolo[3,4-*d*]pyrimidine system (N^1 atom in the pyrazole ring). As a result, we anticipated ring closure with participation of N^5.

Intramolecular electrophilic cyclization of 6-allylsulfanyl derivatives **IIa** and **IIb** by the action of iodine in chloroform gave the corresponding angular tricyclic pentaiodides **IIIa** and **IIIb**. The reaction time was 14 days at room temperature (yield 65%), while the cyclization of other pyrimidine systems is known to be complete in 2 days (yield >90%) [6–8]. Salts **IIIa** and **IIIb** were converted into 1-aryl-8-iodomethyl-7,8-dihydro-4*H*-pyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-ones **IVa** and **IVb** by treatment with sodium sulfite. Compounds **IVa** and **IVb** did not undergo dehydroiodination on heating with morpholine at 70°C; this fact differentiates them from analogous thiazolopyrimidinone derivatives which readily lose hydrogen iodide under similar conditions [6–8]. On the other hand, treatment of **IVb** with sodium acetate in DMSO at 70°C gave 8-methylidene derivative **Vb**. Increased stability of iodomethyl derivatives **IVa** and **IVb** to

Scheme 1.



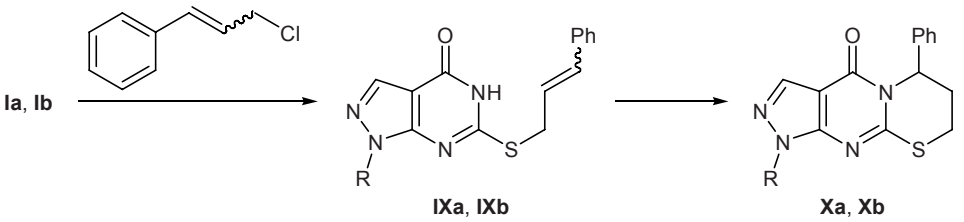
R = Ph (**a**), 4-MeC_6H_4 (**b**).

dehydroiodination is likely to be related to steric hindrances created by the aryl substituent on N^1.

The structure of compound **IVb** was unambiguously determined by X-ray analysis. Crystals of pyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one **IVb** belong to centrosymmetric space group (Fig. 1). The bicyclic pyrazolopyrimidine fragment is almost planar due to conjugation: the mean-square deviation of atoms from the plane is 0.017 Å; the S^1, C^6, and C^7 atoms of the dihydrothiazole ring deviate from that plane by 0.195, –0.100, and 0.302 Å, respectively, and the C^9–C^{14} benzene ring is turned through a dihedral angle of 62.0° with respect to the pyrazolopyrimidine fragment. The C^5–S^1 [1.735(2) Å] and C^6–S^1 bonds [1.802(3) Å] are nonequivalent because of different hybridizations of the C^5 and C^6 atoms, and the bond angle distribution in the pyrimidin-4-one fragment is somewhat unusual, although it remains fairly typical [12–14] of structurally related heterocycles. Thus the endocyclic bond angles at C^4 and N^4 are appreciably reduced to 115.49(18) and 114.96(16)°, respectively, whereas the endocyclic angle at C^5 is increased to 127.69(19)° relative to the ideal value for conjugated six-membered heterocycles (120°). No conjugate intermolecular contacts were detected in crystal.

6-Allylsulfanylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **IIa** and **IIb** in the presence of concentrated sulfuric acid underwent intramolecular cyclization to give angular 7,8-dihydro-4*H*-pyrazolo[4,3-*e*][1,3]thiazolo-[3,2-*a*]pyrimidin-4-one derivatives **VIa** and **VIb**.

Scheme 2.



R = Ph (**a**), 4-MeC_6H_4 (**b**).

6-(Prop-2-yn-1-ylsulfanyl)pyrazolopyrimidinone **VIIb** was obtained by alkylation of compound **Ib** with prop-2-yn-1-yl bromide. The reaction of **VIIb** with concentrated sulfuric acid also afforded compound **Vb**, and the exocyclic double bond in the latter failed to migrate into the thiazole ring even on prolonged heating in concentrated sulfuric acid at 70°C. On the other hand, the use of sodium methoxide as condensing agent changes the direction of cyclization of compound **VIIb**, and the product is linearly fused pyrazolo[3,4-*d*][1,3]thiazolo[3,2-*a*]pyrimidinone **VIIIb**. We believe that the primary cyclization product is 6-methylidene derivative **A** which undergoes double bond migration to give compound **VIIIb**.

By alkylation of 6-thioxopyrazolopyrimidinones **Ia** and **Ib** with cinnamyl chloride we obtained the corresponding 6-(3-phenylprop-2-en-1-ylsulfanyl) derivatives **IXa** and **IXb** (Scheme 2). Compounds **IXa** and **IXb** failed to react with iodine, but they readily underwent intramolecular ring closure by the action of concentrated sulfuric acid with formation of linearly fused 7,8-dihydro-4*H*,6*H*-pyrazolo[3′,4′:4,5]pyrimido[2,1-*b*]-[1,3]thiazin-4-ones **Xa** and **Xb**. Obviously, in this case the cyclization involved the N^5 atom of the pyrazolopyrimidine system.

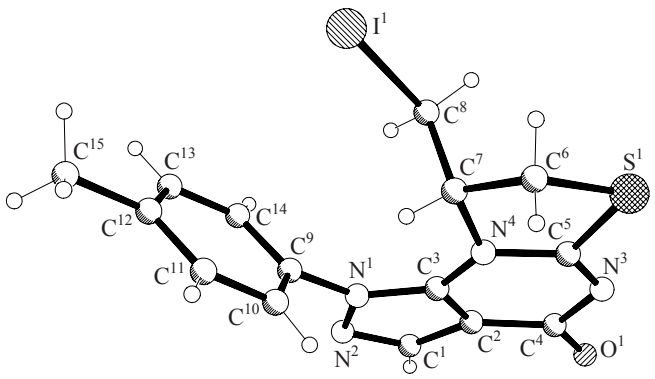
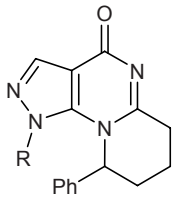


Fig. 1. Structure of the molecule of 8-iodomethyl-1-(4-tolyl)-1,4,7,8-tetrahydropyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (**IVb**) according to the X-ray diffraction data. Principal bond lengths (Å) and bond angles (deg): N^1–N^2 1.378(3), C^1–N^2 1.308(3), C^3–N^1 1.342(3), C^1–C^2 1.396(3), C^2–C^3 1.370(3), C^2–C^4 1.436(3), C^3–N^4 1.361(3), C^4–O^1 1.216(3), C^4–N^3 1.394(3), C^5–N^3 1.278(3), C^5–N^4 1.373(2), C^5–S^1 1.735(2), C^6–S^1 1.802(3), C^6–C^7 1.517(3), C^7–N^4 1.470(2), C^8–I^1 2.126(2); $C^1N^2N^1$ 104.97(19), $C^3N^1N^2$ 110.06(18), $N^1C^3N^4$ 130.23(17), $N^1C^3C^2$ 108.56(18), $N^2C^1C^2$ 112.6(2), $C^3C^2C^1$ 103.8(2), $N^3C^4C^2$ 115.49(18), $C^3N^4C^5$ 114.96(16), $N^4C^3C^2$ 121.21(18), $C^3C^2C^4$ 120.8(2), $N^3C^5N^4$ 127.69(19), $C^5N^3C^4$ 119.71(18), $C^5S^1C^6$ 92.10(10).

However, the formation of angular products like **XI** in the cyclization of **IXa** and **IXb** cannot be ruled out. Structures **X** and **XI** possess similar spin systems; therefore, they cannot be distinguished on the basis of the ^1H and ^{13}C NMR spectra. To solve this problem, we recorded HMQC and HMBC heteronuclear ^{13}C–^1H correlation (through one and 2–3 chemical bonds, respectively) spectra of compound **Xb** (see table).



XIa, **XIb**

In order to assign ^{13}C signals using heteronuclear correlation data, it was necessary to identify the ^1H NMR signals first. It was fairly easy to do on the basis of the signal multiplicities. Further confirmations were made using two-dimensional COSY and NOESY techniques. Correlations through one chemical bond in the HMQC spectrum allowed us to reliably assign signals from carbon atoms linked to hydrogen, and quaternary carbon atoms were identified by analysis of correlations through 2–3 chemical bonds in the HMBC spectrum. Here, the most important was correlation between the 5-H proton in the thiazine ring (δ 6.28 ppm) and C^4 in the pyrimidine ring (δ_C 156.8 ppm). Such correlation is possible only when compound **Xb** has linear structure. Figure 2 shows the chemical shifts of protons and carbon nuclei in molecule **Xb**, as well as the principal correlations in the HMBC spectrum of

Xb. It was interesting that the HMBC spectrum revealed no correlation between 3-H in the pyrazole ring (δ 8.23 ppm) and carbonyl carbon atom in the pyrimidine ring, which are separated by three chemical bonds. A probable reason is that the corresponding coupling constant is close to zero. Analogous pattern was observed in the spectra of other structurally related compounds.

In the IR spectra of angular tricyclic compounds **IVa**, **IVb**, **Vb**, **VIa**, and **VIb**, absorption bands due to stretching vibrations of the carbonyl group are located in the region 1660–1665 cm^{-1}, while linearly fused derivatives **VIIIb**, **Xa**, and **Xb** displayed carbonyl absorption bands at 1715 (**VIIIb**) and 1700 cm^{-1} (**X**). These data are consistent with those reported in [6–8] for angular and linear thiazolo(thiazino)pyrimidinones. Compound **IIIb** was characterized by a carbonyl absorption frequency of 1740 cm^{-1} in the IR spectrum.

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 on a Varian VXR-300 spectrometer (300 MHz) using tetramethylsilane as internal reference; the ^{1}H NMR spectrum of compound **Xb** was also recorded in $CDCl_3$ on a Varian Mercury-400 instrument (400 MHz).

The X-ray diffraction data for a single crystal of compound **IVb**, 0.2×0.3×0.50 mm, were acquired at room temperature on a Bruker Smart Apex II diffractometer (λMoK_α irradiation, graphite monochromator, θ_{max} = 31.17°, spherical segment $-13 \le h \le 13$, $-11 \le k \le 11$, $-31 \le l \le 32$). Monoclinic crystals, space group $P2_1/n$ (no. 14); $C_{15}H_{13}IN_4OS$; M 424.25; unit cell parameters: a = 8.900(2), b = 7.800(2), c = 22.213(6) Å; β = 95.432(4)°; V = 1535.1(7) Å^3; Z = 4; d_{calc} = 1.836 g/cm^3; μ = 2.229 mm^{-1}; F(000) = 832. Total of 11150 reflections were measured, 4560 of which were independent (averaging factor R = 0.0183). The structure was solved by the direct method and was refined by the full-matrix least-squares procedure in anisotropic approximation using SHELXS97 and SHELXL97 software packages [15, 16]. The refinement procedure was performed using 3577 reflections with $I > 2\sigma(I)$ (240 refined parameters, 14.9 reflections per parameter); the weight scheme $\omega = 1/[\sigma^2(Fo^2) + (0.0329P)^2 + 0.6135R]$ was applied, where $R = (Fo^2 + 2Fc^2)/3$; the ratio of the maximal (average) shift and the error in the last iteration was 0.014 (0.000). All hydrogen atoms were visualized objectively from

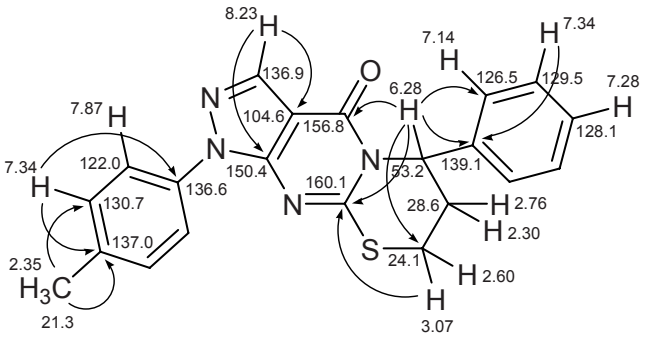


Fig. 2. Correlations in the HMBC spectrum of 6-phenyl-1-(4-tolyl)-4,6,7,8-tetrahydro-1*H*-pyrazolo[3′,4′:4,5]pyrimido-[2,1-*b*][1,3]thiazin-4-one (**Xb**).

Fourier difference series, and their positions were refined in isotropic approximation; only hydrogen atom in the methyl group ($C^{15}H_3$) were localized on the basis of geometry considerations. The final divergence factors were R_1 = 0.0429 and wR_2 = 0.0743, goodness of fit 1.044 (for all independent reflections), and R_1 = 0.0294, wR_2 = 0.0696, GOF = 1.044 [for reflections with $I > 2\sigma(I)$]. The residual electron density from the Fourier difference series after the last iteration was 0.77 and –0.72 e/Å^3. The complete set of crystallographic data for compound **Xb** was deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 664997).

6-Allylsulfanyl-1-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones IIa and IIb (*general procedure*). Compound **Ia** or **Ib**, 4 mmol, and allyl bromide,

Heteronuclear ^{13}C–^{1}H correlations in the NMR spectra of 6-phenyl-1-(4-tolyl)-4,6,7,8-tetrahydro-1*H*-pyrazolo-[3′,4′:4,5]pyrimido[2,1-*b*][1,3]thiazin-4-one (**Xb**)

δ_H, ppm	HMQC, δ_C, ppm	HMBC, δ_C, ppm
8.23	136.9	150.4, 104.6
7.87	122.0	137.0, 130.3, 122.0
7.34	130.3, 129.5	139.1, 136.5, 130.3, 129.5, 126.1, 122.0, 21.3
7.28	128.1	129.5, 126.1
7.14	126.1	129.5, 128.1, 126.1, 53.2
6.28	52.2	160.1, 156.8, 139.1, 126.1, 24.1
3.07	24.1	53.2, 160.1
2.75	28.6	24.1
2.60	24.1	28.6
2.35	28.6	137.0, 130.3, 122.0
2.30	21.3	–

0.41 ml (4.7 mmol), were added in succession to a solution of 0.188 g (4.7 mmol) of sodium hydroxide in 30 ml of ethanol, and the mixture was stirred for 1 h on heating under reflux. The mixture was cooled, and the precipitate was filtered off and washed with water and ethanol.

6-Allylsulfanyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IIa). Yield 0.87 g (77%), mp 237°C (from ethanol–DMSO). ^{1}H NMR spectrum, δ, ppm: 3.92 d (2H, CH_2, J = 6.6 Hz), 5.17 d (1H, CH, J = 10.5 Hz), 5.34 d (1H, CH, J = 16.8 Hz), 5.93–6.07 m (1H, CH), 7.41 t (1H, H_{arom}, J = 7.5 Hz), 7.58 t (2H, H_{arom}, J = 7.5 Hz), 8.08 d (2H, H_{arom}, J = 7.8 Hz), 8.26 s (1H, CH), 12.75 s (1H, NH). Found, %: C 59.09; H 4.19; N 19.63; S 11.31. $C_{14}H_{12}N_4OS$. Calculated, %: C 59.14; H 4.25; N 19.70; S 11.28.

6-Allylsulfanyl-1-(4-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IIb). Yield 1.07 g (90%), mp 254–255°C (from ethanol–DMSO). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.89 d (2H, CH_2, J = 6.3 Hz), 5.16 d (1H, CH, J = 10.2 Hz), 5.32 d (1H, CH, J = 17.4 Hz), 5.91–6.05 m (1H, CH), 7.36 d (2H, H_{arom}, J = 7.8 Hz), 7.92 d (2H, H_{arom}, J = 8.1 Hz), 8.22 s (1H, CH), 12.70 s (1H, NH). Found, %: C 60.34; H 4.63; N 18.70; S 10.90. $C_{15}H_{14}N_4OS$. Calculated, %: C 60.38; H 4.73; N 18.78; S 10.75.

1-Aryl-8-iodomethyl-7,8-dihydro-1*H*-pyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-ones IVa and IVb (*general procedure*). A solution of 0.76 g (3 mmol) in 50 ml of chloroform was added under stirring to a solution of 1 mmol of compound **IIa** or **IIb** in 20 ml of chloroform. The mixture was stirred for 14 days at room temperature, and the precipitate of salt **IIIa** or **IIIb** was filtered off and washed with chloroform. The product was dissolved in 10 ml of DMSO, a 5% aqueous solution of sodium sulfite was added until the mixture turned colorless, and the pale yellow precipitate was filtered off, washed with water, and recrystallized from ethanol–DMSO.

8-Iodomethyl-4-oxo-1-(4-tolyl)-4,5,7,8-tetrahydro-1*H*-pyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-9-ium pentaiodide (IIIb). Yield 0.71 g (67%), mp 275°C (decomp.). IR spectrum, ν, cm^{-1}: 1740 (C=O), 1595, 1550, 1225, 1060. ^{1}H NMR spectrum, δ, ppm: 2.44 s (3H, CH_3), 2.90 d (1H, CH, J = 11.1 Hz), 3.19 t (1H, CH, J = 10.8 Hz), 3.38 d (1H, CH, J = 12.0 Hz), 3.84–3.90 m (1H, CH), 4.64–4.71 m (1H, CH), 7.46 d (2H, H_{arom}, J = 7.8 Hz), 7.62 d (2H, H_{arom}, J = 7.5 Hz), 8.20 s (1H, CH). Found, %: C 16.84; H 1.35; I 71.53; N 5.21; S 2.96. $C_{15}H_{14}I_6N_4OS$. Calculated, %: C 17.00; H 1.33; I 71.85; N 5.29; S 3.03.

8-Iodomethyl-1-phenyl-1,4,7,8-tetrahydropyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (IVa). Yield 0.34 g (83%), mp 230°C (decomp.; from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 1660 (C=O), 1590, 1560, 1475, 1410, 1240, 1195. ^{1}H NMR spectrum, δ, ppm: 2.91 d (1H, CH, J = 10.8 Hz), 3.18 t (1H, CH, J = 10.5 Hz), 3.34 d (1H, CH, J = 11.7 Hz), 3.80–3.86 m (1H, CH), 4.61–4.68 m (1H, CH), 7.62–7.69 m (3H, H_{arom}), 7.71–7.77 m (2H, H_{arom}), 8.17 s (1H, CH). Found, %: C 40.73; H 2.65; I 30.81; N 13.54; S 7.73. $C_{14}H_{11}IN_4OS$. Calculated, %: C 40.99; H 2.70; I 30.93; N 13.66; S 7.82.

8-Iodomethyl-1-(4-tolyl)-1,4,7,8-tetrahydropyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (IVb). Yield 0.37 g (87%), mp 242°C (decomp., ethanol–DMSO). IR spectrum, ν, cm^{-1}: 1660 (C=O), 1590, 1560, 1480, 1435, 1410, 1240, 1200. ^{1}H NMR spectrum, δ, ppm: 2.44 s (3H, CH_3), 2.91 d (1H, CH, J = 9.6 Hz), 3.18 t (1H, CH, J = 10.8 Hz), 3.33 d (1H, CH, J = 11.7 Hz), 3.80–3.86 m (1H, CH), 4.61–4.67 m (1H, CH), 7.44 d (2H, H_{arom}, J = 7.8 Hz), 7.62 d (2H, H_{arom}, J = 8.4 Hz), 8.14 s (1H, CH). Found, %: C 42.34; H 3.14; I 29.82; N 13.13; S 7.58. $C_{15}H_{13}IN_4OS$. Calculated, %: C 42.46; H 3.09; I 29.91; N 13.21; S 7.56.

8-Methylidene-1-(4-tolyl)-1,4,7,8-tetrahydropyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (Vb). *a*. Anhydrous sodium acetate, 0.05 g (0.65 mmol), was added to a solution of 0.21 g (0.5 mmol) of compound **IVb** in 5 ml of DMSO, and the mixture was stirred for 3 h at 70°C. The mixture was cooled and poured into water, and the precipitate was filtered off and washed with water.

b. Compound **VIIb**, 0.30 g (1 mmol), was dissolved in 5 ml of concentrated sulfuric acid, and the solution was left to stand for 14 h. It was then poured onto ice and neutralized with sodium hydroxide, and the precipitate was filtered off, washed with water, and recrystallized from ethanol–DMSO. Yield 0.11 g (74%, *a*), 0.27 g (91%, *b*), mp 304–306°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 1660 (C=O), 1585, 1550, 1485, 1345, 1220, 1190. ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 4.13 s (2H, CH_2), 4.21–4.22 m (1H, CH), 4.87–4.88 m (1H, CH), 7.32 d (2H, H_{arom}, J = 8.7 Hz), 7.47 d (2H, H_{arom}, J = 8.4 Hz), 8.27 s (1H, CH). Found, %: C 60.82; H 3.99; N 18.96; S 10.75. $C_{15}H_{12}N_4OS$. Calculated, %: C 60.79; H 4.08; N 18.91; S 10.82.

1-Aryl-8-methyl-1,4,7,8-tetrahydropyrazolo[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-ones VIa and

VIb were synthesized as described above for compound **Vb** (method *b*).

8-Methyl-1-phenyl-1,4,7,8-tetrahydropyrazolo-[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (VIa). Yield 0.26 g (92%), mp 280°C (decomp., from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 1660 (C=O), 1590, 1555, 1470, 1405, 1240, 1200. ^{1}H NMR spectrum, δ, ppm: 0.96 d (3H, CH_3, J = 6.0 Hz), 3.13 d (1H, CH, J = 11.4 Hz), 3.74–3.80 m (1H, CH), 4.55–4.64 m (1H, CH), 7.59–7.77 m (5H, H_{arom}), 8.17 s (1H, CH). Found, %: C 59.25; H 4.19; N 19.77; S 11.19. $C_{14}H_{12}N_4OS$. Calculated, %: C 59.14; H 4.25; N 19.70; S 11.28.

8-Methyl-1-(4-tolyl)-1,4,7,8-tetrahydropyrazolo-[4,3-*e*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (VIb). Yield 0.29 g (97%), mp >300°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 1665 (C=O), 1605, 1575, 1485, 1420, 1250, 1220. ^{1}H NMR spectrum, δ, ppm: 0.97 d (3H, CH_3, J = 6.6 Hz), 2.43 s (3H, CH_3), 3.12 d (1H, CH, J = 11.4 Hz), 3.72–3.78 m (1H, CH), 4.55–4.64 m (1H, CH), 7.42 d (2H, H_{arom}, J = 7.8 Hz), 7.61 d (2H, H_{arom}, J = 8.1 Hz), 8.14 s (1H, CH). Found, %: C 60.51; H 4.81; N 18.67; S 10.69. $C_{15}H_{14}N_4OS$. Calculated, %: C 60.38; H 4.73; N 18.78; S 10.75.

6-(Prop-2-yn-1-ylsulfanyl)-1-(4-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (VIIb). Compound **Ib**, 0.98 g (4 mmol), was added to a solution of 0.19 g (4.8 mmol) of sodium hydroxide in 30 ml of ethanol, 0.36 ml (4 mmol) of a 80% solution of prop-2-yn-1-yl bromide in toluene was then added, and the mixture was stirred for 1 h on heating under reflux. The mixture was cooled, and the precipitate was filtered off and washed with water and ethanol. Yield 1.04 g (88%), mp 261–262°C. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.29 t (1H, CH, J = 3.0 Hz), 4.06 d (2H, CH_2, J = 2.4 Hz), 7.35 d (2H, H_{arom}, J = 8.4 Hz), 8.05 d (2H, H_{arom}, J = 8.4 Hz), 8.24 s (1H, CH), 12.79 s (1H, NH). Found, %: C 60.72; H 4.03; N 18.98; S 10.73. $C_{15}H_{12}N_4OS$. Calculated, %: C 60.79; H 4.08; N 18.91; S 10.82.

6-Methyl-1-(4-tolyl)-1*H*-pyrazolo[3,4-*d*][1,3]thiazolo[3,2-*a*]pyrimidin-4-one (VIIIb). A mixture of 0.15 g (0.5 mmol) of compound **VIIb** and 0.017 g (0.75 mmol) of sodium in 15 ml of methanol was stirred for 5 days at room temperature. The precipitate was filtered off and washed with water and methanol. Yield 0.05 g (34%), mp 226–227°C. IR spectrum, ν, cm^{-1}: 1715 (C=O), 1530, 1395, 1190, 1155, 1095. ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 2.71 s (3H, CH_3), 6.92 s (1H, CH), 7.34 d (2H, H_{arom}, J = 8.1 Hz), 7.90 d (2H, H_{arom}, J = 8.1 Hz), 8.29 s (1H, CH). Found, %: C 60.94; H 4.07; N 18.83; S 10.87. $C_{15}H_{12}N_4OS$. Calculated, %: C 60.79; H 4.08; N 18.91; S 10.82.

1-Aryl-6-(3-phenylprop-2-en-1-ylsulfanyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones IXa and IXb (*general procedure*). Compound **Ia** or **Ib**, 4 mmol, was added to a solution of 0.19 g (4.8 mmol) of sodium hydroxide in 25 ml of ethanol, 0.67 ml (4.8 mmol) of cinnamyl chloride was then added, and the mixture was stirred for 1 h on heating under reflux. The mixture was cooled, and the precipitate was filtered off and washed with water and ethanol.

1-Phenyl-6-(3-phenylprop-2-en-1-ylsulfanyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IXa). Yield 1.22 g (85%), mp 242°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 4.08 d (2H, CH_2, J = 6.9 Hz), 6.35–6.47 m (1H, CH), 6.65 d (1H, CH, J = 15.6 Hz), 7.2–7.33 m (5H, H_{arom}), 7.38–7.45 m (1H, H_{arom}), 7.55–7.6 m (2H, H_{arom}), 8.09 d (2H, H_{arom}, J = 8.7 Hz), 8.22 s (1H, CH), 12.69 s (1H, NH). Found, %: C 66.54; H 4.37; N 15.59; S 8.86. $C_{20}H_{16}N_4OS$. Calculated, %: C 66.65; H 4.47; N 15.54; S 8.90.

6-(3-Phenylprop-2-en-1-ylsulfanyl)-1-(4-tolyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IXb). Yield 1.06 g (71%), mp 216°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 4.06 d (2H, CH_2, J = 6.9 Hz), 6.36–6.46 m (1H, CH), 6.64 d (1H, CH, J = 15.0 Hz), 7.2–7.29 m (5H, H_{arom}), 7.65 d (2H, H_{arom}, J = 8.4 Hz), 7.94 d (2H, H_{arom}, J = 8.4 Hz), 8.22 s (1H, CH), 12.68 s (1H, NH). Found, %: C 67.48; H 4.87; N 14.91; S 8.51. $C_{21}H_{18}N_4OS$. Calculated, %: C 67.36; H 4.85; N 14.96; S 8.56.

1-Aryl-6-phenyl-4,6,7,8-tetrahydro-1*H*-pyrazolo-[3′,4′:4,5]pyrimido[2,1-*b*][1,3]thiazin-4-ones Xa and Xb were synthesized as described above for compound **Vb** (method *b*) from pyrazolopyrimidines **IXa** and **IXb**, respectively.

1,6-Diphenyl-4,6,7,8-tetrahydro-1*H*-pyrazolo-[3′,4′:4,5]pyrimido[2,1-*b*][1,3]thiazin-4-one (Xa). Yield 0.20 g (56%), mp 192°C (from ethanol). IR spectrum, ν, cm^{-1}: 1705 (C=O), 1530, 1440, 1400, 1190, 1130, 1080. ^{1}H NMR spectrum, δ, ppm: 2.27–2.40 m (1H, CH), 2.58–2.69 m (1H, CH), 2.75–2.84 m (1H, CH), 3.07–3.15 m (1H, CH), 6.31 s (1H, CH), 7.17 d (2H, H_{arom}, J = 6.9 Hz), 7.27–7.44 m (4H, H_{arom}), 7.56–7.61 m (2H, H_{arom}), 8.04 d (2H, H_{arom}, J = 8.1 Hz), 8.29 s (1H, CH). Found, %: C 66.73; H 4.49; N 15.43; S 8.82. $C_{20}H_{16}N_4OS$. Calculated, %: C 66.65; H 4.47; N 15.54; S 8.90.

6-Phenyl-1-(4-tolyl)-4,6,7,8-tetrahydro-1*H*-pyrazolo[3′,4′:4,5]pyrimido[2,1-*b*][1,3]thiazin-4-one (Xb). Yield 0.18 g (48%), mp 181–182°C (from ethanol). IR spectrum, ν, cm^{-1}: 1705 (C=O), 1535, 1450, 1400, 1200, 1130. ^1H NMR spectrum, δ, ppm: 2.28–2.42 m (4H, CH_3, CH), 2.58–2.68 m (1H, CH), 2.76–2.84 m (1H, CH), 3.07–3.15 m (1H, CH), 6.3 s (1H, CH), 7.16 d (2H, H_{arom}, J = 7.2 Hz), 7.28–7.42 m (5H, H_{arom}), 7.90 d (2H, H_{arom}, J = 8.1 Hz), 8.26 s (1H, CH). Found, %: C 67.21; H 4.71; N 15.01; S 8.50. $C_{21}H_{18}N_4OS$. Calculated, %: C 67.36; H 4.85; N 14.96; S 8.56.

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